Rubinstein-Taybi syndrome: Dental manifestations and management

T S Roberts, M BCh, MChD, M Chetty, BSc, BChD, MChD; I Stephen, BChD, PhD; M Urban, MB BCh, FCPaed (SA), MMed; K Fieggen, MB ChB, FCPaed (SA); P Beighton, MD, PhD, FRCPE

Case reports

The major manifestations of Rubinstein-Taybi syndrome (RSTS) (OMIM 180849), also referred to as the ‘broad thumb-hallux syndrome’ and ‘multiple congenital anomalies/mental retardation syndrome’, are a characteristic facies, broad thumbs and great toes, stunted stature and mental retardation. Dental changes are a minor, yet significant component of the condition. Craniofacial growth retardation in RSTS is frequently complicated by unerupted teeth, while dental caries is related to the inherent intellectual deficit. Dental problems necessitate interdisciplinary management in terms of oral surgery, conservative dentistry, periodontics and orthodontics. When affected individuals are unco-operative, certain dental procedures may warrant general anaesthesia. In these instances, dental and medical staff will combine their expertise to enhance the well-being of the patient. In addition, specific dental changes may alert the medical practitioner to the possible diagnosis of RSTS. In this article we document the oro-dental manifestations and review the oro-dental approach in the management of three patients with RSTS. Our experience in South Africa may be relevant to other countries at a similar stage of development.
rubinstein and Taybi[1] documented the distinctive features of RSTS in a French orthopaedic journal. In 1963, unaware of the aforementioned report, Rubinstein and Taybi[1] documented the syndromic association of broad thumbs and toes with facial abnormalities, thereby delineating the condition that now bears their conjoined eponym.

Prophylactic scaling and polishing would be undertaken at the same time. The parents were presented with the treatment plan and given guidance concerning the importance of oral hygiene. However, they declined treatment.

Case 3
A boy of mixed ancestry and aged 7 years, previously diagnosed as having RSTS, was referred to the Faculty of Dentistry at Tygerberg Hospital, Parow, Cape Town, for dental assessment. He had the typical features of the syndrome, notably intellectual impairment, short stature, a bulbous nose and broad terminal phalanges of the thumb (Fig. 4) and halluces. No other family member was affected.

His developmental milestones were delayed and he had been bottle-fed until the age of 2 years. He started crawling at this stage and walked at the age of 4 years. By the age of 7 years he could only speak approximately 10 words and communication with him at the dental clinic was difficult. It was impossible to proceed with radiographic investigations due to his mental impairment.

Intra-oral examination revealed that he had a high-arched palate and several carious teeth. His dentition was otherwise unremarkable. He was a mouth breather and his oral hygiene was poor.

During the first visit, mother and child were given instruction in oral hygiene and his diet was analysed. The boy was not co-operative in the dental chair, but it was possible to apply topical fluoride to the teeth. Regular follow-up visits indicated that his oral health status had improved significantly. His dental age was within the normal range for his age. His dental age was within the normal range for his age.

The teeth were noted to be malaligned in the maxillary and mandibular arches, with an angulation and inclination within the normal range, while the mandibular incisors were retroclined and retruded.

Routine chromosomal analysis did not reveal any abnormality. Molecular techniques, including fluorescence in situ hybridisation (FISH) testing and sequencing of the CREBBP gene, can be used to confirm the clinical diagnosis of RSTS, but are currently not available in South Africa.

Case 2
A South African black girl born in 2003 was diagnosed as having RSTS at 20 months of age and followed up regularly at Red Cross War Memorial Children’s Hospital, Cape Town, until the age of 4 years. Her family history was negative.

She was born at term following a pregnancy complicated by hyperemesis gravidarum. She had no significant medical illnesses, but her developmental milestones were severely delayed: she started walking at 2 years of age and spoke her first words at 3 years of age.

Her growth was retarded with height below the third centile and weight on the third centile. She was microcephalic and had typical facial features of RSTS, including down-sloping palpebral fissures, a beaked nose with the columella extending below the alae nasae, a prominent lower lip and a grimacing appearance of the mouth. The palate was high-arched. The terminal phalanges of all fingers were broad, while both thumbs and halluces were strikingly broad. She had a slight pectus excavatum and mild thoracolumbar scoliosis. Radiological examination revealed six lumbar vertebrae.

The teeth were noted to be malaligned at 2½ years of age, and several required extraction for caries resulting from prolonged bottle-feeding (nursing caries). On follow-up one year later, several of the remaining teeth were carious.

At the age of 4 years, the patient had multiple carious teeth, associated with poor dental hygiene. Her dental age was within the normal range. Since several teeth in all four quadrants of her mouth required extraction, arrangements were made for this to be done under general anaesthesia.

Discussion
In 1957, Michail et al.[8] described a 7-year-old boy with the distinctive features of RSTS in a French orthopaedic journal. In 1963, unaware of the aforementioned report, Rubinstein and Taybi[1] documented the syndromic association of broad thumbs and toes with facial abnormalities, thereby delineating the condition that now bears their conjoined eponym.

A mutation in the CREBBP gene (OMIM 600140) at the chromosomal locus 16p13.3 was
is detectable by the FISH technique in about 15% of persons with RSTS (RSTS1). With sequence analysis, this figure rises to 30-50%. In a minority of individuals, the EP300 gene (OMIM 602700) at 22q13 has been implicated (RSTS2). Considerable intragenic heterogeneity has been recognised in both forms of RSTS. In general, the craniofacial abnormalities and intellectual impairment are more severe in RSTS1 than in RSTS2.

The severity of the manifestations of RSTS is very variable, and the case reports presented in this article provide a perspective of the range of involvement. It is relevant that management, including dental measures, is determined by the severity, or otherwise of the feature in question. The main practical problem in RSTS is mental retardation, and affected persons are normally incapable of independent existence and adequate self-care. Guidelines for the general surveillance and medical management of the RSTS have been proposed by Wiley et al. Considerations pertaining to dental management include the use of general anaesthesia if cardiac or respiratory abnormalities are present. Possible challenges during intubation result from anterior positioning and mechanical inadequacies or weakening of the larynx, and there is a risk of aspiration pneumonia. Cardiac abnormalities and arrhythmias have been reported in RSTS, and if present, require evaluation before conservative or invasive dental treatment. Skeletal and soft-tissue changes in the head and neck region resulting in upper-airway obstruction can lead to mouth breathing and recurrent pneumonia.

The oral features of RSTS have been reviewed extensively by Hennekam and Van Doorne andBloch-Zupan et al., and are mentioned by several other authors. Dental talon cusps are present in a high proportion of persons with RSTS, but this feature was absent in our patients. All three had high-arched palates – often associated with malocclusion and tooth malalignment. Hypo- and hyperdontia may also occur. Caries resulting from inadequate dental hygiene is frequent, and in older children may be the result of the intellectual disability and motor impairment that characterise the syndrome. Problems with feeding during early development could be the cause of the nursing caries in cases 2 and 3.

Optimal oral and dental health is of the utmost importance in the general well-being of a patient with RSTS. Good oral health enables problem-free assimilation and digestion of food, which translates to a physically healthy individual. Caries and periodontal disease affect quality of life. If individuals with RSTS cannot articulate coherently, they may suffer from dental pain for weeks or months. In turn, this may affect their eating habits, resulting in malnutrition and an impaired immune response. Bleeding gums may prevent caregivers or parents from continuing routine oral hygiene practices, and together with halitosis may result in social isolation and poor self-esteem.

Proposed management protocols

The dental treatment plan that we proposed for patient 1 encompassed 6-monthly follow-up visits for monitoring the eruption of the remaining teeth. As she showed no signs of a space discrepancy, surgical exposure and assisted eruption would have been unwarranted. Subsequent radiographs showed evidence of eruption with open root apices. Maxillary arch expansion for the correction of the bilateral posterior cross-bite was undertaken. In addition, the anterior teeth were levelled and aligned, where necessary, to facilitate the eruption of the canine and premolar teeth in their appropriate positions. A fixed lingual arch-wire was placed in the mandibular arch to maintain the space for the erupting canine and premolar teeth.

In view of her age and the developmental status of her dentition, patient 2 would ideally have been recalled at 6-monthly intervals to enable adequate monitoring of her growth and development.

Management of patient 3 was difficult because of the severity of his intellectual impairment. Extractions and conservative treatment were undertaken under general anaesthesia without complications. The boy returned to the dental clinic every 6 months for cleaning and prophylaxis.

Conclusion

The oro-dental complications of RSTS are important but neglected aspects of the disorder. On the basis of our experience in Cape Town it has become apparent that the multifaceted problems necessitate a team approach towards dental management and possible anaesthesia. Equally, in an environment where facilities may be suboptimal, multidisciplinary collaboration is crucial for effective management and for the well-being of the affected person.

Ethics approval. Ethics approval was obtained from the Human Research Ethics Committee, Faculty of Health Sciences, UCT.

Acknowledgements. Support for this project was received by PB from the South African Medical Research Council and the National Research Foundation.

References